**Metadata**

**Manuscript:** Liver weight changes induced in mice and rats by chemical exposures: Derivation of critical level sizes from the Toxicity Reference Database (ToxRefDB).

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Dataset(s) title:

**Absolute (ALW) and relative (RLW) liver weight changes and associated histopathologic changes in the livers of rodents exposed to chemicals relative to control groups.**

Dataset(s) description:

This dataset was prepared from the US Environmental Protection Agency's (EPA) Toxicity Reference Database (ToxRefDB) that contains information for 1,142 chemicals and 5,960 studies. Curations include information regarding the study design, chemical identity, dosing, treatment group parameters, treatment-related (significantly different from control) and critical (adverse) effects for all dose treatment groups, as well as endpoint testing status according to guideline specifications.

ToxRefDB data was examined for all subchronic (SUB) studies with complete curations, which included registrant-submitted toxicity studies from the US EPA’s Office of Pesticide Programs (OPP) and guideline studies sourced from the National Toxicology Program (NTP).

Statistically significant differences between treatment and control group data at p<0.05 within the source documents was extracted and denoted with a “treatment-related” Boolean indicator “true”. Across the studies with absolute liver weights and relative-to-body (RLW) liver weights, the treatment-related mean effect values at the lowest effect (LE) dose levels as well as mean control liver weights were determined for all chemical-study-sex-species-exposure route groupings. The LE-ALW and LE-RLW changes were quantified as effect size differences from control using the following equation:

Effect\_size = 100 x (LE Effect\_value – Control Effect\_Value) / Control Effect\_Value

Any microscopic liver pathology effects occurring at the corresponding LE dose level of weight change were also identified and listed in the dataset. Histopathology terms were presented as they appeared in ToxRefDB without harmonizing different hierarchical levels and aggregating multiple terms used to depict the same lesions.

The final dataset that includes chemical stressor information, study source identifiers, study type, sex, species, strain, administration route, administration method, dose level, mg/kg/day value, qualitative and quantitative effect information, effect size from control, and pathology effects if present. The dataset includes data from 389 subchronic studies on 273 chemicals.

Definition(s) of acronyms and abbreviations:

* LE-ALW: absolute liver weight at the lowest effect dose
* LE-RLW: relative liver weight (liver-to-body) at the lowest effect dose

Definition(s) of data variables and column headings:

* **preferred\_name:** Name of the test substance.
* **study\_id:** Autoincremented unique identifier for each study in the database.
* **study\_source\_id:** Document identifier provided by the study source.
* **sex:** Gender of test animal.
* **species:** Species of test animal used.
* **strain:** Intraspecific description of group of animals used in a study; generally, a stock of animals that share a uniform morphological or physiological character, or group that is genetically uniform.
* **admin\_route:** Path by which test substance is administered to animal. Options include oral, dermal, inhalation, injection, or other.
* **admin\_method:** Specific path by which the test substance was administered via the administration route. Examples include capsule, diet, gavage, or topical.
* **dose\_level:** Numeric rank indicating the level of dose administered to test animals, with lower dose levels indicating lower concentrations of a chemical, e.g., 0 = vehicle, 1 = lowest dose, etc. The dose level for some studies may be staggered since concentrations may vary by sex, e.g., male treatment group: 0 = vehicle, 1 = lowest dose, 3 = second lowest dose, etc.
* **mg\_kg\_day\_value:** The mg/kg/day species-specific converted value, usually converted from ppm concentration.
* **endpoint\_category:** The broadest descriptive term for an endpoint. Possible endpoint categories include: systemic, developmental, reproductive, and cholinesterase.
* **endpoint\_type:** The subcategory for endpoint\_category, which is more descriptive for a particular endpoint, e.g. pathology gross, clinical chemistry, reproductive performance, etc.
* **endpoint\_target:** More specific description than endpoint\_type, often indicating where or how the sample was collected to supply data for a particular endpoint. Target may describe an organ, tissue, metabolite, or protein measured.
* **effect\_desc:** Specific description for an effect, usually detailing a specific condition associated with an endpoint\_target, e.g. dysplasia, atrophy, necrosis, etc.
* **dtg\_effect\_comment:** NULL if no additional comment needed. Field provides additional explanation of the dose-treatment group-effect row in the table, including statistical significance.
* **treatment\_related:** Boolean description for an effect by dose treatment group. “TRUE” indicates there was a statistically significant difference from the control group for the effect; “FALSE” indicates there was no difference from control group. The highest dose level at which no significant observable adverse effects were observed corresponds to the no effect level (NEL). The lowest effect level (LEL) can be inferred by treatment related effects.
* **critical\_effect:** Boolean description for an effect by dose treatment group. “TRUE” corresponds to a toxic or adverse effect denoted in the study summary or via expert judgement using a weight-of-evidence approach. “FALSE” indicates that although an effect is produced at this level, it is not considered adverse, nor immediate precursors to specific adverse effects. If there are several critical effects, the no observed adverse effect level (NOAEL) is determined from the highest dose level without critical effects. The lowest dose level at which the critical effect was observed in a study is the lowest observed adverse effect level (LOAEL.)
* **effect\_val:** Numeric value of a measured effect; can be continuous or dichotomous (incidence) data.
* **effect\_val\_unit:** Unit associated with the effect value.
* **effect\_var:** Measurement of the variance for a set of data associated with a measured effect, generally reported as the standard deviation (SD) or standard error (SE).
* **effect\_var\_type:** Name of the variance metric used to determine the effect variance, typically the standard deviation (SD) or standard error (SE). Other effect\_var types include: interquartile range, 95% confidence limit, and none.
* **sample\_size:** Number of animals used for an examination for a particular effect.
* **effect\_size:** *Corresponds to LE-ALW or LE-RLW as defined in the Dataset description section*
* **pathology\_liver\_effect\_descriptions:** List of histopathological effect\_desc associated at same dose level as *LE-ALW or LE-RLW.*

Units of measurements:

* Effect\_size: %
* All other variables have units of measurements described in specific columns

Meaning of variables (e.g., data dictionary):

Described in definition of data variables.

Descriptions of sample types

Each line corresponds to a single chemical-species-sex-route of administration and shows LE-ALW or LE-RLW values and associated histopathologic changes